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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/340,196	06/28/1999	RYOJI KATO	990701	3596

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1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/340,196	Applicant(s) Kato et al.
	Examiner Jennifer Hunt	Art Unit 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 19, 2001* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *49-77* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *49-77* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

Response to Amendment

1. Claims 49-77 are pending in the application and addressed herein.

Claim Rejections Maintained

2. The rejection of claims 49-77 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of detecting sugar chain variations in thyroglobulin molecules, does not reasonably provide enablement for methods of differentiating any of "two types" of thyroglobulins' and methods of diagnosing cancer is maintained for reasons of record.

As set forth in the previous Office Action, mailed 7/5/2001, factors to be considered in determining scope and enablement are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented in the specification, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability of the unpredictability of the art, and 8) the breadth of the claims (see Ex parte Forman, 230 USPQ 546, BPAI, 1986).

The claims are broadly drawn to methods of detecting "one of two types" of thyroglobulins, using an antibody which binds to both types of thyroglobulins and an antibody or lectin which binds to only one of the two types.

The specification discloses a specific method in which a constant region, common to human thyroglobulins is bound by an antibody and subsequently a lectin which binds to a sugar chain is used to determine thyroglobulin sugar chain variants which correspond to malignancies.

The claims broadly encompass differentiating any number of different types of thyroglobulin by binding to a sugar chain molecule, however sorting thyroglobulins by sugar chain variations would not differentiate any "type" of thyroglobulin, by rather only those that have a detectable difference in their sugar chain structure. Any "type" of thyroglobulin could refer to other non-sugar chain modifications, sequence variations, or even production in distinct species, etc. Detection of sugar chain molecule variations would not be indicative of the broadly claimed "types" of thyroglobulins.

Additionally, with regard to the claims which recite diagnosis of a malignancy, use of specific lectins which are known to bind to sugar chain modifications in the thyroglobulins of cancer patients would be required to diagnose cancer. The claims broadly recite any antibody or lectin, regardless of what it binds, many of which would in no way correlate to malignancy and thus would not function unless the appropriate lectins were used.

Thus the disclosure of one art known method of detecting thyroglobulin sugar chain variants is insufficient support under the first paragraph of 35 U.S.C 112 for claims which encompass differentiating any type of thyroglobulin from any other type, including those yet undiscovered. The courts have held that:

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based In some way on his teachings, since some improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence, not In compliance with the first paragraph of U.S.C. 112; that paragraph requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill In the art; In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement In the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; In cases involving unpredictable factors, such as chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."In re Fisher 427 F.2d 833, 166 USPQ 18 (CCPA 1970)

Therefor one of skill in the art would not be enabled to practice the invention commensurate in scope with the claims.

Applicant's arguments are summarized as:

a. Applicant argues that the examiner's rejection does not appear to be drawn to enablement, and that the examiner's remarks incorrectly state that thyroglobulins having different sugar chain molecules are not in fact distinct molecules. Applicant argues that the instant specification and claims are functionally defining different "types" of thyroglobulins based on binding properties of the sugar molecule of the thyroglobulin, and further that one of ordinary skill in the art could easily obtain the anti-thyroglobulin antibodies and lectins recited in the claims, and use them in the methods of the claims.

b. With regard to the claims drawn to detecting malignancy, applicant argues that the claims are not overly broad in reciting that any lectin/antibody combination could be used to detect malignancy, because "how medically accurate the determination resulting from performing the method is, is not an enablement issue".

c. Applicant last suggests that perhaps the examiner intended to reject the claims under 35 U.S.C. 101, as having an "unbelievable utility".

Applicant's arguments filed 11-19-2001 have been fully considered but they are not persuasive.

a. With regard to the detection of different "types" of thyroglobulin, as set forth in the previous office action, the instantly claimed methods are drawn to methods of detecting only sugar chain variations, and thus only distinguish between one specific subclass of thyroglobulin molecules and fails to differentiate between thyroglobulins which are different "types" but which do not express distinct sugar chains, such as thyroglobulins of different sequences, species, or with

different modifications. The examiner acknowledges that the instant specification defines thyroglobulin molecules having distinct sugar chain molecules as different "types" of thyroglobulins. The claims are not limited to detecting different sugar chain variant thyroglobulins, and thus encompass numerous thyroglobulins which could not necessarily be distinguished by different sugar chains.

b. With regard to the detection of malignancy, "how medically accurate" the instantly claimed methods are does matter for enablement, because one of skill in the art must be able to use the invention without undue experimentation. If "a method of diagnosing malignancy" is not medically accurate, one of skill in the art would not be able to use the invention without undue experimentation.

c. The claimed invention has utility. To be considered "useful" an invention need only have one useful embodiment. In the instant case, there are functioning and useful embodiments of the invention. These useful embodiments, however, are not commensurate in scope with the claims, for the reasons set forth above.

3. The rejection of claims 49-66, 68-75, and 77 under 35 U.S.C. 103(a) as being unpatentable over Hanham et al. Biochemica et Biophysica Acta, Vol 884, 1986, in view of Voller et al. Rul. World Health Organ., Vol. 53, pages 55-65, 1976, or Harlow and Lane

Antibodies, a Laboratory Manuel, Chapter 14, pages 553-612, 1988 or Samuel et al., US Patent 5,242,799, September 7, 1993 is maintained for reasons of record.

As set forth in the previous Office Action, Hanham et al. teaches a method of measuring types of thyroglobulin and detecting malignancy in a fluid sample originating from a living body (a tissue sample which has been homogenized in PBS)(see methods, page 159) and the corresponding reagent. The method of Hanham et al. uses an anti-thyroglobulin antibody which is capable of binding to both types of thyroglobulin and further using a lectin (see for example "Lectin Affinity electrophoresis", page 160) which is capable of binding a specific sugar chain structure on only one of the two types of thyroglobulins. The method of Hanham et al. measures thyroglobulins using both antibodies and lectins in combination with one another. The methods include competitive binding assays and correlation of glycosylation variants (different types of thyroglobulins) to malignancy. (see pages 160-164, especially results and figures).

Although Hanham et al. does not necessarily specifically recite various order of steps or specific methods of measuring identical properties of the instant claims, those variations would be obvious to one of skill in the art, as routine art known variants of identical methods. For example, see Voller et al., or Harlow and Lane, both of which discuss the numerous assay methods encompassed by the instant claims. See also Samuel et al., US Patent 5,242,799, September 7, 1993, which discusses numerous lectin/antibody assays (columns 1-6). Further, it is obvious to alter the order in which steps of a known method are performed:

MPEP 2144.04 See In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

Therefor it would have been *prima facie* obvious to one of ordinary skill in the art to modify the assay of Hanham et al. by varying the assay with art known assay techniques taught by Voller et al., or Harlow and Lane, or Samuel et al for the purpose of efficiency and convenience.

Applicant's arguments are summarized as:

a. Hanham et al. does not teach adding an antibody or a lectin to a fluid sample, but rather describes preparing gels containing an antibody or lectin, through which thyroglobulins are electrophoresed.

b. Hanham et al. does not require that the antibody and the lectin are added to the same fluid sample simultaneously.

c. Hanham et al. describes a qualitative measurement, not a quantitative measurement.

d. Samuel et al. teaches away from the instant method, by teaching that the lectin my bind to the antigen independently of the antibody.

e. Voller et al. and Harlow and Lane teach general immunoassays only and fail to address the specifics of the instant invention.

Applicant's arguments filed 11-19-2001 have been fully considered but they are not persuasive.

a. Hanham et al. does teach a fluid sample from a living body from which thyroglobulins are measured. The antibodies and lectins are added to the fluid sample when the sample is mixed with the gels.

b. The fluid sample is mixed with both antibody and lectin simultaneously. The claims do not require the thyroglobulin be simultaneously in contact with the antibody and the lectin.

c. The method of Hanham et al. is described as "allowing characterization of small quantities of thyroglobulin"(see abstract, for example). This is a quantitative measurement.

d. Samuel et al. is merely cited as an example of an assay which combines lectins and antibodies. A skilled artisan recognizes that lectins, antibodies or combinations thereof can be combined to detect a molecule, and or modifications of that molecule, and that selection of antibodies or lectins which do or do not cross block each other will vary depend on which are known immunoassay is being utilized. Samuel et al. makes it clear that when one is using a "sandwich" method, the lectin or antibody combination should bind simultaneously. Although Samuel et al. does not implicitly state that cross blocking could be used to select different modifications, this is well established in the art and would be appreciated by one of skill in the art. Further, that the lectin will not bind to a molecule which is bound by an antibody is not commensurate in scope with the argued claims which do not recite such.

e. Voller et al. and Harlow and Lane are merely cited to demonstrate the vast repetiore of art known quantitative immunoassay combinations, since the instant claims encompass a broad range of subcombinations of a method.

4. The rejection of claims 49-66, 68-75, and 77 under 35 U.S.C. 103(a) as being unpatentable over Helig et al., Endocrinol. Suppl., 108(267), page 151, 1985, in view of Voller et al. Rul. World Health Organ., Vol. 53, pages 55-65, 1976, or Harlow and Lane Antibodies, a Laboratory Manuel, Chapter 14, pages 553-612, 1988 or Samuel et al., US Patent 5,242,799, September 7, 1993 is maintained for reasons of record.

As set forth in the previous Office Action, Helig et al. teaches a method of measuring types of thyroglobulin and detecting malignancy in a fluid sample originating from a living body and the corresponding reagent. The method of Helig et al. uses an anti-thyroglobulin antibody which is capable of binding to both types of thyroglobulin and further using an additional which is capable of binding a specific sugar chain structure on only one of the two types of thyroglobulins. The methods include competitive binding assays and correlation of variants (different types of thyroglobulins) to malignancy. (see entire document)

Although Helig et al. does not necessarily specifically recite various order of steps or specific methods of measuring identical properties of the instant claims, those variations would be obvious to one of skill in the art, as routine art known variants of identical methods. For example, see Voller et al., or Harlow and Lane, both of which discuss the numerous assay methods encompassed by the instant claims. See also Samuel et al., US Patent 5,242,799, September 7, 1993, which discusses numerous lectin/antibody assays (columns 1-6). Further, it is obvious to alter the order in which steps of a known method are performed:

MPEP 2144.04 See In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

Therefor it would have been *prima facie* obvious to one of ordinary skill in the art to modify the assay of Helig et al. by varying the assay with art known assay techniques taught by Voller et al., or Harlow and Lane, or Samuel et al for the purpose of efficiency and convenience.

Applicant argues that Heilig et al. fails to detect different species, but rather detects different epitopes of the same thyroglobulin, and merely suggests looking for different species.

Applicant's arguments filed 11-19-2001 have been fully considered but they are not persuasive.

Applicant's arguments are not commensurate in scope with the claims. As set forth above, the claims are drawn to detecting any sugar chain variation, which would encompass the "minimal variations of the fine structure of large molecules" as is taught in Heilig et al. Further, some antibodies which bind to an eiptope on a thyroglobulin would be unable to bind to that epitope on a different species of thyroglobulin having a sugar modification due to conformational changes in that thyroglobulin induced by the modification.

5. The rejection of 49-66, 68-75, and 77 under 35 U.S.C. 103(a) as being unpatentable over Wang et al., Chung-hua Ping Li Hsueh Tsa Chin, Volume 19, No 2, pages 90-93, in view of Lancet, (1977). Vol. 1, No. 8017, pp. 881-882, and further in view of Voller et al. Rul. World Health Organ., Vol. 53, pages 55-65, 1976, or Harlow and Lane Antibodies, a Laboratory

Manuel, Chapter 14, pages 553-612, 1988, or Samuel et al., US Patent 5,242,799, September 7, 1993 is maintained for reasons of record.

As set forth in the previous Office Action, Wang et al. teaches a method of measuring types of thyroglobulin and detecting malignancy in a tissue sample originating from a living body and the corresponding reagent. The method of Wang et al. uses an anti-thyroglobulin antibody which is capable of binding to both types of thyroglobulin and further using a lectin which is capable of binding a specific sugar chain structure on only one of the two types of thyroglobulins. The method of Wang et al. measures thyroglobulins using both antibodies and lectins in combination with one another. The methods include competitive binding assays and correlation of glycosylation variants (see abstract and full text translation)

Although Wang et al. teaches detection of thyroglobulin in tissues, the detection of thyroglobulin in serum and subsequent correlation to cancer is well known in the art (see for example Lo Gerfo et al., Lancet, (1977). Vol. 1, No. 8017, pp. 881-882)

Although Wang et al. does not necessarily specifically recite various order of steps or specific methods of measuring identical properties of the instant claims, those variations would be obvious to one of skill in the art, as routine art known variants of identical methods. For example, see Voller et al., or Harlow and Lane, both of which discuss the numerous assay methods encompassed by the instant claims. See also Samuel et al., US Patent 5,242,799, September 7, 1993, which discusses numerous lectin/antibody assays (columns 1-6). Further, it is obvious to alter the order in which steps of a known method are performed:

MPEP 2144.04 See In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

Therefor it would have been prima facie obvious to one of ordinary skill in the art to modify the assay of Wang et al. and Lo Gerfo et al., by varying the assay with art known assay techniques taught by Voller et al., or Harlow and Lane, or Samuel et al for the purpose of efficiency and convenience.

Applicant's arguments are summarized as:

a. Wang et al. does not indicate what the lectins binding to the thyroglobulin are.

b. Wang et al. does not indicate lectins are binding to Tg.

c. Wang et al. does not differentiate distinct types of thyroglobulin.

d. Wang et al. does not allow measurement of the amount of thyroglobulin.

e. LoGerfo fails to supplement the lack of teaching of detection of multiple types of thyroglobulin

Applicant's arguments filed 11-19-2001 have been fully considered but they are not persuasive.

Initially, it is noted that Wang et al. is not an abstract, but rather the translation of a full length paper.

a. The specific lectins are indicated in table 2.

b. The Tg bound by the lectins are indicted in table 4, and pages 9-10 of the translation.

c. The differentiation of thyroglobulins by lectin binding is indicated in table 4 and pages 9-10 of the translation.

d. Amounts of thyroglobulin bound are discussed in table 4, at pages 9-10, and at page 13 of the translation.

e. Wang et al. does teach the detection and quantification of multiple type of thyroglobulin as set forth above, and thus LoGerfo need only teach that thyroglobulin is detectable in serum.

6. The rejection of claims 49, 50, 52, and 57-65 under 35 U.S.C. 103(a) as being unpatentable over Canfield et al., WO 87/00289, published January 15, 1987, in view of Voller et al. Rul. World Health Organ., Vol. 53, pages 55-65, 1976, or Harlow and Lane Antibodies, a Laboratory Manuel, Chapter 14, pages 553-612, 1988, or Samuel et al., US Patent 5,242,799, September 7, 1993 is maintained for reasons of record.

As set forth in the previous Office Action, WO 87/00289 teaches a method of measuring types of thyroglobulin in a fluid sample originating from a living body and the corresponding reagent. The method of WO 87/00289 uses an anti-thyroglobulin antibody which is capable of binding to both types of thyroglobulin and further using a lectin which is capable of binding a specific sugar chain structure on only one of the two types of thyroglobulins. The method of WO 87/00289 measures thyroglobulins using both antibodies and lectins in combination with one another. The methods include competitive binding assays. (see especially pages 9-15)

Although WO 87/00289 does not necessarily specifically recite various order of steps or specific methods of measuring identical properties of the instant claims, those variations would be obvious to one of skill in the art, as routine art known variants of identical methods. For example, see Voller et al., or Harlow and Lane, both of which discuss the numerous assay methods encompassed by the instant claims. See also Samuel et al., US Patent 5,242,799, September 7, 1993, which discusses numerous lectin/antibody assays (columns 1-6). Further, it is obvious to alter the order in which steps of a known method are performed:

MPEP 2144.04 See In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

Therefor it would have been prima facie obvious to one of ordinary skill in the art to modify the assay of WO 87/00289 by varying the assay with art known assay techniques taught by Voller et al., or Harlow and Lane, or Samuel et al for the purpose of efficiency and convenience.

Applicant's arguments are summarized as:

a. WO 87/00289 does not teach detection of thyroglobulin.

b. WO 87/00289 does not teach measurement of the amount of conjugate which is formed

c. WO 87/00289 does not teach "anti thyroglobulin antibody-2" which cannot bind to the thyroglobulin to which a specific antibody or lectin is already bound.

Applicant's arguments filed 11-19-2001 have been fully considered but they are not persuasive.

a. WO 89/00289 does teach measurement of thyroglobulin (see page 9, line 21).

b. WO 87/00289 does teach measurement of the amount of conjugate (see page 12, line 7-24).

c. WO 89/00289 does teach the various methods of differentiating different proteins in assays, all of which are known in the art as set forth previously, and further which are discussed at pages 13-15.

7. The rejection of claims 49-66, 68-75, and 77 under 35 U.S.C. 103(a) as being unpatentable over Canfield et al., WO 87/00289, published January 15, 1987, in view of Tarutani et al., Journal of Biochemistry, Volume 98, No. 3, 1985, or Wang et al., Chung-hua Ping Li Hsueh Tsa Chin, Volume 19, No 2, pages 90-93, or Hanham et al. Biochemica et Biophysica Acta, Vol 884, 1986, or Helig et al., Endocrinol. Suppl., 108(267), page 151, 1985, and further in view of Voller et al. Rul. World Health Organ., Vol. 53, pages 55-65, 1976, or Harlow and Lane Antibodies, a Laboratory Manuel, Chapter 14, pages 553-612, 1988, or Samuel et al., US Patent 5,242,799, September 7, 1993 is maintained for reasons of record.

As set forth in the previous Office Action, WO 87/00289 teaches a method of measuring types of thyroglobulin in a fluid sample originating from a living body and the corresponding reagent. The method of WO 87/00289 uses an anti-thyroglobulin antibody which is capable of binding to both types of thyroglobulin and further using a lectin which is capable of binding a specific sugar chain structure on only one of the two types of thyroglobulins. The method of WO

87/00289 measures thyroglobulins using both antibodies and lectins in combination with one another. The methods include competitive binding assays. (see especially pages 9-15)

WO 87/00289 fails to specifically correlate sugar chain variants to cancer, however that variation in thyroglobulin sugar chains is indicative of cancer is well established in the art. See for example, Tarutani et al., or Wang et al., or Hanham et al., or Helig et al. (see for example, abstracts).

Further, although WO 87/00289 does not necessarily specifically recite various order of steps or specific methods of measuring identical properties of the instant claims, those variations would be obvious to one of skill in the art, as routine art known variants of identical methods. For example, see Voller et al., or Harlow and Lane, both of which discuss the numerous assay methods encompassed by the instant claims. See also Samuel et al., US Patent 5,242,799, September 7, 1993, which discusses numerous lectin/antibody assays (columns 1-6). Further, it is obvious to alter the order in which steps of a known method are performed:

MPEP 2144.04 See In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

Therefor it would have been prima facie obvious to one of ordinary skill in the art to modify the assay of WO 87/00289 by varying the assay to correlate to cancer, as taught by Tarutani et al., Wang et al., Hanham et al., or Helig et al. with art known assay techniques taught by Voller et al., or Harlow and Lane, or Samuel et al for the purpose of efficiency and convenience.

Applicant's arguments are summarized as:

a. Tarutani et al. does not teach the recited method of binding of an antibody to Tg and comparison of Tg ratios for the diagnosis of malignancy.

b. Tarutani et al. fails to supplement the deficiencies of the other references.

Applicant's arguments filed 11-19-2001 have been fully considered but they are not persuasive.

a. Tarutani et al. is cited to demonstrate that it is known in the art that carbohydrate (sugar chain) modifications of Tg are known in the art to correlate to carcinoma, regardless of which art known immunoassay is utilized to measure them.

b. The other references are not deficient, as set forth above.

8. The rejection of claims 49-77 under 35 U.S.C. 103(a) as being unpatentable over Canfield et al., WO 87/00289, published January 15, 1987, in view of Tarutani et al., Journal of Biochemistry, Volume 98, No. 3, 1985, or Wang et al., Chung-hua Ping Li Hsueh Tsa Chin, Volume 19, No 2, pages 90-93, or Hanham et al. Biochemica et Biophysica Acta, Vol 884, 1986, or Helig et al., Endocrinol. Suppl., 108(267), page 151, 1985, and further in view of Voller et al. Rul. World Health Organ., Vol. 53, pages 55-65, 1976, or Harlow and Lane Antibodies, a Laboratory Manuel, Chapter 14, pages 553-612, 1988, or Samuel et al., US Patent 5,242,799 and further in view of Larena, et al., Langenbecks Archiv fur Chrurgie Vol 381/2 pages 102-113 1996 is maintained for reasons of record.

As set forth in the previous Office Action, WO 87/00289, and Tarutani et al., Wang et al., Hanham et al., or Helig et al., and Voller et al., or Harlow and Lane, or Samuel et al. teach as set forth above and applied to claims 49-66, 68-75, and 77 supra. WO 87/00289, and Tarutani et al., Wang et al., Hanham et al., or Helig et al., and Voller et al., or Harlow and Lane, or Samuel et al. fail to teach an anti-thyroglobulin antibody reactive with a Lewis type sugar chain.

Larena et al. teaches that Lewis type sugar chains are known in the art to be useful for detection of malignancy, including thyroid malignancy. Larena compares levels to total thyroglobulin to Lewis expressing thyroglobulin as well as normal thyroid tissue to cancerous tissue.

Therefor it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the antibody of Larena et al. as the anti-thyroglobulin antibody in the methods of any of WO 87/00289, and Tarutani et al., Wang et al., Hanham et al., or Helig et al., and Voller et al., or Harlow and Lane, or Samuel et al. because the antibody is detectable in normal and cancerous tissue and useful for determination of thyroid malignancy as set forth in Larena et al.

Applicant argues that Larena fails to discuss that the sugar antigens are part of thyroglobulin.

Applicant's arguments filed 11-19-2001 have been fully considered but they are not persuasive.

As set forth in previous Office Actions, and above, Larena compares levels to total thyroglobulin to Lewis expressing thyroglobulin as well as normal thyroid tissue to cancerous tissue.

Conclusion

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Hunt, whose telephone number is (703) 308-7548. The examiner can normally be reached Monday through Thursday 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached at (703) 308-3995. The fax number for the group is (703) 305-3014 or (703) 308-4242.

Communications via internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**anthony.caputa@uspto.gov**].

All internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists the possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist, whose telephone number is (703) 308-0196.

Sheela J. Huff
SHEELA HUFF
PRIMARY EXAMINER

Jennifer Hunt

February 11, 2002